

WHAT IS CLAIMED IS:

1. An isolated nucleic acid encoding a polypeptide monomer comprising an alpha subunit of a heteromeric potassium channel, the polypeptide monomer:

(i) having the ability to form, with at least one additional Kv alpha subunit, a heteromeric potassium channel having the characteristic of voltage gating;

(ii) having a monomer subunit association region that has greater than about 70% amino acid sequence identity to a Kv6.2 subunit association region; and

(iii) specifically binding to polyclonal antibodies generated against SEQ ID NO:1 or SEQ ID NO:17.

2. The isolated nucleic acid of claim 1, wherein the nucleic acid encodes human Kv6.2.

3. The isolated nucleic acid of claim 1, wherein the nucleic acid encodes mouse Kv6.2.

4. The isolated nucleic acid of claim 1, wherein the nucleic acid encodes SEQ ID NO:1 or SEQ ID NO:17.

5. The isolated nucleic acid sequence of claim 1, wherein the nucleic acid has a nucleotide sequence of SEQ ID NO:2 or SEQ ID NO:18.

6. The isolated nucleic acid of claim 1, wherein the nucleic acid is amplified by primers that selectively hybridize under stringent hybridization conditions to the same sequence as the primer sets selected from the group consisting of:

ATGCCCATGTCTTCCAGAGACAGG (SEQ ID NO:3),

GATGTCTAGAGGGAGTTACATGTAGCG (SEQ ID NO:4) and

GGCACTACGCATCCTCTACGTAATGCGC (SEQ ID NO:5),

GATGATGGCCCCACCAATAGGATGCGG (SEQ ID NO:6) and  
ATGCCCATGCCTTCCAGAGACGG (SEQ ID NO:7),  
TTACATGTGCATGATAGGCAAGGCTG (SEQ ID NO:8) and  
GTCCAGGCCCAAGACAAGTGTCAG (SEQ ID NO:9),  
5 GGGAGAAGGTGTGGAAGATAGACG (SEQ ID NO:10).

7. The isolated nucleic acid of claim 1, wherein the nucleic acid  
encodes a polypeptide monomer having a molecular weight of about between 53 kDa to  
about 65 kDa.

10 8. An isolated nucleic acid encoding a polypeptide monomer comprising an  
alpha subunit of a heteromeric potassium channel, the polypeptide monomer:

(i) having the ability to form, with at least one additional Kv alpha subunit, a  
heteromeric potassium channel having the characteristic of voltage gating;

15 (ii) having an S4-S6 region that has greater than about 85% amino acid sequence  
identity to a Kv6.2 S4-S6 region and

(iii) specifically binding to polyclonal antibodies generated against SEQ ID NO:1  
or SEQ ID NO:17.

20 9. An isolated nucleic acid encoding a polypeptide monomer that  
specifically hybridizes under stringent conditions to SEQ ID NO:2 or SEQ ID NO:18.

10. The isolated nucleic acid of claim 1 or 8, wherein said nucleic  
acid selectively hybridizes under moderately stringent hybridization conditions to a  
25 nucleotide sequence of SEQ ID NO:2 or SEQ ID NO:18.

11. An isolated polypeptide monomer comprising an alpha subunit of  
a heteromeric potassium channel, the polypeptide monomer:

(i) having the ability to form, with at least one additional Kv alpha subunit, a  
30 heteromeric potassium channel having the characteristic of voltage gating;

- (ii) having a monomer subunit association region that has greater than 70% amino acid sequence identity to a Kv6.2 subunit association region; and
- (iv) specifically binding to polyclonal antibodies generated against SEQ ID NO:1 or SEQ ID NO:17.

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12. The isolated polypeptide monomer of claim 11, wherein the polypeptide monomer has an amino acid sequence of human Kv6.2.

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13. The isolated polypeptide monomer of claim 11, wherein the polypeptide monomer has an amino acid sequence of mouse Kv6.2.

14. The isolated polypeptide monomer of claim 11, wherein the polypeptide monomer has an amino acid sequence of SEQ ID NO:1 or SEQ ID NO:17.

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15. An isolated polypeptide monomer comprising an alpha subunit of a heteromeric potassium channel, the polypeptide monomer:

(i) having the ability to form, with at least one additional Kv alpha subunit, a heteromeric potassium channel having the characteristic of voltage gating;

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(ii) having an S4-S6 region that has greater than 85% amino acid sequence identity to a Kv6.2 S4-S6 region; and

(iii) specifically binding to polyclonal antibodies generated against SEQ ID NO:1 or SEQ ID NO:17.

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16. An antibody that selectively binds to the polypeptide monomer of claim 11 or 15.

17. An antibody of claim 16, wherein the polypeptide monomer has an amino acid sequence of SEQ ID NO:1 or SEQ ID NO:17.

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18. An expression vector comprising the nucleic acid of claim 1.

19. A host cell transfected with the vector of claim 18.

20. A method for identifying a compound that increases or decreases  
5 ion flux through a heteromeric voltage-gated potassium channel, the method comprising the steps of:

(i) contacting the compound with a eukaryotic host cell or cell membrane in which has been expressed a polypeptide monomer comprising an alpha subunit of a heteromeric potassium channel, the polypeptide monomer:

10 (a) having the ability to form, with at least one additional Kv alpha subunit, a heteromeric potassium channel having the characteristic of voltage gating;

(b) having a monomer subunit association region that has greater than 70% amino acid sequence identity to a Kv6.2 subunit association region; and

15 (c) specifically binding to polyclonal antibodies generated against SEQ ID NO:1 or SEQ ID NO:17; and

(ii) determining the functional effect of the compound upon the cell or cell membrane expressing the potassium channel.

21. The method of claim 20, wherein the increased or decreased flux  
20 of ions is determined by measuring changes in current or voltage.

22. The method of claim 20, wherein the potassium channel monomer polypeptide is recombinant.

25 23. The method of claim 20, wherein the potassium channel monomer polypeptide is human Kv6.2.

24. The method of claim 20, wherein the potassium channel monomer polypeptide is mouse Kv6.2.

25. The method of claim 20, wherein the potassium channel monomer polypeptide has an amino acid sequence of SEQ ID NO:1 or SEQ ID NO:17.

26. A method for identifying a compound that increases or decreases ion flux through a heteromeric voltage-gated potassium channel, the method comprising the steps of:

(i) contacting the compound with a eukaryotic host cell or cell membrane in which has been expressed a polypeptide monomer comprising an alpha subunit of a heteromeric potassium channel, the polypeptide monomer:

(a) having the ability to form, with at least one additional Kv alpha subunit, a heteromeric potassium channel having the characteristic of voltage gating;

(b) having an S4-S6 region that has greater than 85% amino acid sequence identity to a Kv6.2 S4-S6 region; and

(c) specifically binding to polyclonal antibodies generated against SEQ ID NO:1 or SEQ ID NO:17; and

(ii) determining the functional effect of the compound upon the cell or cell membrane expressing the potassium channel.

27. A method of detecting the presence of Kv6.2 in mammalian tissue, the method comprising the steps of:

(i) isolating a biological sample;

(ii) contacting the biological sample with a Kv6.2-specific reagent that selectively associates with Kv6.2; and,

(iii) detecting the level of Kv6.2-specific reagent that selectively associates with the sample.

28. The method of claim 27, wherein the Kv6.2-specific reagent is selected from the group consisting of: Kv6.2 specific antibodies, Kv6.2 specific oligonucleotide primers, and Kv6.2 nucleic acid probes.

29. The method of claim 27, wherein the sample is from a human.

30. In a computer system, a method of screening for mutations of human Kv6.2 genes, the method comprising the steps of:

5 (i) entering into the computer a first nucleic acid sequence encoding an voltage-gated potassium channel polypeptide monomer having a nucleotide sequence of SEQ ID NO:2, SEQ ID NO:18, and conservatively modified versions thereof;

(ii) comparing the first nucleic acid sequence with a second nucleic acid sequence having substantial identity to the first nucleic acid sequence; and

10 (iii) identifying nucleotide differences between the first and second nucleic acid sequences.

31. The method of claim 30, wherein the second nucleic acid sequence is associated with a disease state.

15 32. In a computer system, a method for identifying a three-dimensional structure of Kv6.2 polypeptide monomers, the method comprising the steps of:

(i) entering into the computer system an amino acid sequence of at least  
20 25 amino acids of a potassium channel polypeptide monomer or at least 75 nucleotides of a gene encoding the polypeptide monomer, the polypeptide monomer having an amino acid sequence of SEQ ID NO:1 or SEQ ID NO:17, and conservatively modified versions thereof; and

(ii) generating a three-dimensional structure of the polypeptide monomer  
25 encoded by the amino acid sequence.

33. The method of claim 32, wherein said amino acid sequence is a primary structure and wherein said generating step includes the steps of:

(i) forming a secondary structure from said primary structure using energy terms  
30 determined by the primary structure; and

(ii) forming a tertiary structure from said secondary structure using energy terms determined by said secondary structure.

34. The method of claim 33, wherein said generating step further  
5 includes the step of forming a quaternary structure from said tertiary structure using anisotropic terms encoded by the tertiary structure.

35. The method of claim 31, further comprising the step of  
identifying regions of the three-dimensional structure of a Kv6.2 potassium channel  
10 protein that bind to ligands and using the regions to identify ligands that bind to the potassium channel protein.